

## REVIEW

# Examination of the nutritional intake of patients undergoing opioid replacement therapy: A systematic review

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## Abstract

**Aim:** This systematic review aimed to determine the level of existing research that investigates the intake, specifically macro and micronutrient intake, of patients undergoing opioid replacement therapy.

**Methods:** A systematic review was conducted across PubMed, Embase, Cochrane and CINAHL databases using a pre-determined protocol. Studies published between 2001 and 2022 assessing macronutrient or micronutrient intake in opioid replacement therapy patients were included. The Strengthening the Reporting of Observational Studies in Epidemiology checklist was utilised for quality appraisal. Data from each of the included papers was synthesised in a narrative manner. Data extracted included all measurements of nutrition including macronutrient, and micronutrient intake and any bioanalysis results and methods utilised.

**Results:** Seven papers (one cohort study and six cross-sectional studies,  $n = 443$ ) were included that investigated an aspect of nutritional intake in patients receiving opioid replacement therapy. The majority of included papers reported an assessment of both macro and micronutrient and resulting energy intake as determined by food consumption. The included papers described a picture of irregular nutritional intake in patients undergoing opioid replacement therapy.

**Conclusion:** Minimal research into the nutritional intake of opioid replacement therapy patients exists. The existing research is suggestive of irregular nutritional intake from both macro and micronutrient consumption and indicates a need for further studies and increased attention on this vulnerable patient group.

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**KEYWORDS**

dietary intake, nutrition, opioid replacement therapy, recovery, systematic review

## 1 | INTRODUCTION

Opioid use disorder is a recognised international public health issue affecting several countries globally.<sup>1,2</sup> There are an estimated 15.6 million opioid dependent people worldwide and the international consumption of opioids is believed to be increasing.<sup>3</sup> In Australia, each day approximately 150 hospitalisations involve opioid harm and three people die from drug-induced deaths involving opioid use.<sup>1</sup> In the United States, between 2000 and 2014, approximately half a million people died from a drug overdose, with opioids accounting for 61% of all drug-related overdoses in 2014.<sup>2</sup> In Australia, the overall rate of codeine-related deaths increased from 3.5 per million in 2000 to 8.7 per million in 2009 with deaths attributed to accidental overdoses found to be more common (48.8%) than intentional deaths (34.7%).<sup>4</sup> The opioid crisis has also affected Canada, who attributed 2861 deaths to opioids in 2016 with an average of 16 Canadians hospitalised each day due to opioid-related poisonings in 2016.<sup>5</sup> In Europe, especially the United Kingdom, there has also been an upward trend in the prescription of opioids and related mortality in recent years.<sup>6</sup>

Poor nutritional health among opioid addicted individuals is well established and a number of studies exist that demonstrate an increased likelihood of severe nutritional deficiencies in this population.<sup>7</sup> Patients with opioid use disorders have been observed to lack nutritional knowledge which leads to unhealthy eating behaviours.<sup>7</sup> Opioid addicted individuals have been shown to have a higher predisposition to the consumption of sweet foods and to consume less than the minimum amount of vegetable, fruit and grains recommended by relevant guidelines.<sup>8,9</sup> Several studies have demonstrated that the consumption of vegetables and fruit in opioid addicted individuals is less than the general population and that these individuals are prone to consume food with low vitamin content.<sup>7,8</sup>

Patients with opioid use disorders have also been shown to suffer from weight loss and irregular changes in dietary patterns.<sup>7</sup> When actively using opioids, individuals report little interest in food, preferring quick and cheap convenience foods.<sup>10</sup> Conversely, when abstaining from opioid use, there is evidence of binge eating disorders.<sup>11</sup> A predisposition to unhealthy eating behaviours in these individuals has been demonstrated and has been shown to be related to a lack of nutritional knowledge and food preparation skills relative to the general population.<sup>7,12</sup> Although the role of nutrition in detoxification

has not been well defined, reports have suggested that an improvement in the nutrition of individuals with opioid use disorders may assist in the recovery process.<sup>7,8,13</sup>

Corresponding with the rise of opioid use disorders, there has been a subsequent increase in the number of individuals seeking treatment for this condition. The number of individuals being treated for opioid addiction has increased since 1990.<sup>3</sup> To combat the opioid addiction crisis, the use of legal opioid agonists, provided at regular dosing intervals to reduce withdrawal, has been implemented as a form of opioid replacement therapy.<sup>14,15</sup> Opioid replacement therapy has been shown to effectively treat opioid addiction.<sup>14,15</sup> Regular treatment is able to be adjusted to a dose that maintains blood levels of opioid agonists to suitably manage cravings and withdrawal without any associated intoxication.<sup>3</sup> A stable dose of opioid replacement therapy has been shown to lead to health and social benefits for patients, including reducing illicit drug use, criminality and improving both physical and mental health.<sup>3</sup>

The use of opioid replacement therapy is well established as a method to improve patients' mental health and reduce substance use, criminal activity and also mortality.<sup>3</sup> Several international studies exist that have investigated the nutrition-related intake of opioid replacement therapy patients.<sup>16-19</sup> It has been demonstrated that patients who participate in opioid replacement therapy have more favourable outcomes when coupled with appropriate nutritional intake.<sup>7</sup> Overall, however, there appears to be a paucity of research investigating actual nutritional intake rather than investigating nutritional health status through biometrics in this patient group.

Consequently, the aim of this systematic review was to determine the level of existing research that investigates the intake, specifically macro and micronutrient intake, of opioid replacement therapy patients.

## 2 | METHODS

A systematic review was conducted using a pre-determined protocol based on the Cochrane Handbook for Systematic Reviews of Interventions.<sup>20</sup> This review adheres to the PRISMA guidelines.<sup>21</sup> This study is registered with PROSPERO (CRD4202127742). In terms of inclusion criteria, the primary outcome measures of interest of included papers were the following:

The nutritional intake of patients undergoing opioid replacement therapy in a community pharmacy or other government, or non-community pharmacy setting was evaluated through direct assessment of intake or bioanalysis of nutrient levels.

Search terms were formulated using the *PICO* structure. *Participants* (P) included patients undergoing opioid replacement therapy in a community pharmacy or other government, or non-community pharmacy setting. *Intervention* (I) included any assessment of nutritional intake such as via a food frequency questionnaire or food recall type assessment. *Comparisons* (C) included addressed intake intervention versus none in the opioid replacement therapy population, or in a non-opioid replacement therapy population. *Outcomes* (O) included any measurement of macro or micronutrient intake or levels. Papers were excluded if they evaluated patient nutritional status or measured utilised methods that differed to the above such as through anthropometric modelling.

Four electronic databases were searched for articles published in English from January 2001 to February 2022. This timeframe was selected to produce papers that reference the most up-to-date nutritional guidelines for the relevant reference countries. The databases searched were PubMed, Embase, Cochrane and CINAHL and the searches were conducted in April 2022. No restriction on study design was implemented for included papers. An electronic search strategy was constructed to incorporate opioid replacement therapy patients and nutritional intake through implementation of the following search terms:

1. opioid
2. opiate
3. OR/1-2
4. replac\*
5. substitute
6. maintenance
7. treat\*
8. therapy
9. OR/4-8
10. 3 AND 9
11. methadone
12. buprenorphine
13. OR/10-12
14. diet
15. nutri\*
16. intake
17. health
18. OR/14-17
19. 13 AND 18
20. Remove duplicates from 19

The search strategy was constructed through use of the Pubmed database. Search terms encompassed medical subject headings and title words. The search strategy was then implemented across the further databases.

Titles were first screened by one author before abstracts of the identified papers were assessed by two authors against the eligibility criteria. References of relevant papers were also manually examined to identify any additional relevant studies. After reaching agreement, all papers that were deemed potentially relevant based on abstract or title were retrieved in full text to allow further detail assessment against the inclusion criteria. A third reviewer was consulted in the case of disagreement. Full-text screening involved using EndNote and Covidence software to manage and retrieve full texts. Figure 1 offers a schematic representation of this process.

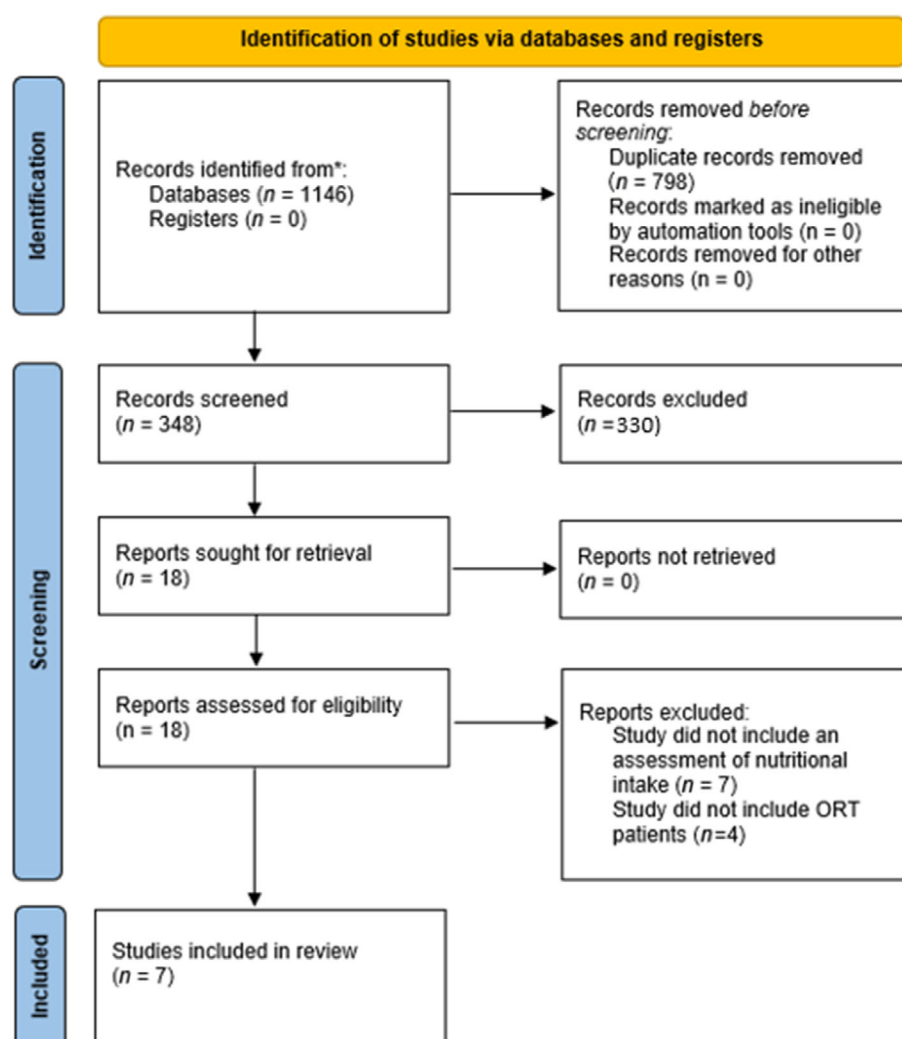
Data from each of the included papers was synthesised in a narrative manner. Data collected included all measurements of nutrition including macronutrient, and micronutrient intake and any bioanalysis results. Methods utilised for the collection of this data was also collected for each included paper. Papers were reviewed by the chief investigator who assessed the individual studies to produce a descriptive summary of characteristics and relevant results. The synthesis of both methods and collected nutritional intake data was tabulated to allow direct comparison. Similarities between included papers and subsequent results was assessed as was the relationships between the included studies.

To appraise the quality of included papers, the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist for observational studies was utilised.<sup>22</sup> The STROBE checklist facilitates the appraisal of methodological quality of six items which are subdivided into 22 criteria. Implementation of the STROBE checklist and assessment of study quality was undertaken independently by two reviewers. A third reviewer was consulted in the case of disagreement.

### 3 | RESULTS

The electronic search process yielded 1142 potential journal articles for inclusion. Of these studies, 934 were excluded based on title screening and duplicate removal. A further 194 papers were retrieved, and abstracts were screened against the inclusion criteria. An additional four papers were identified through reference checking of screened articles. These papers were also assessed against the inclusion criteria. A total of 18 articles were retrieved as full text documents. Eleven were found to be ineligible for inclusion, as they did not satisfy the inclusion criteria of investigating the nutritional intake of patients

FIGURE 1 Study selection flow diagram



undergoing opioid replacement therapy, instead either investigating the nutritional intake of opioid addicted individuals or investigating nutritional knowledge of patients undergoing opioid replacement therapy. Seven studies were included for the final analysis.

Seven studies were included in this review (Table 1). Of these studies, two were conducted in the United States<sup>26,28</sup> and one study was conducted in each of Poland, the United Kingdom, Australia, Portugal and Iran.<sup>9,23-25,27</sup>

Each of the studies investigated an aspect of nutritional intake in opioid replacement therapy patients. Both Shrestha *et al.* and Tomedi *et al.* specifically investigated pregnant women.<sup>26,28</sup> Each of the remaining papers included both female and male participants. The largest patient sample size was investigated by Kheradmand and Kheradmand in their study of 198 individuals.<sup>27</sup> Tomedi *et al.* examined the smallest patient group of 22 patients.<sup>26</sup>

Patients receiving opioid replacement therapy treatment through various institutions were examined in the included research. The papers by Ii *et al.* and Waddington *et al.* examined intake in opioid replacement therapy patients receiving

therapy through community pharmacies.<sup>24,25</sup> Tomedi *et al.*, Alves *et al.* and Kolaryzk *et al.* included patients receiving therapy through single centres, a women's hospital, and a specialised Government department respectively.<sup>9,23,26</sup> Kheradmand and Kheradmand conducted their research across multiple opioid replacement therapy-specific treatment clinics.<sup>27</sup> It was unclear where the patients included in the study by Shrestha *et al.* were receiving their treatment.

Three (Kolarzyk *et al.*, Ii *et al.* and Waddington *et al.*) of the included studies utilised a 24-h food recall to assess nutritional intake of patients.<sup>23-25</sup> The food recall assessment by Kolarzyk *et al.* was completed once at baseline and again following 4 years of opioid replacement therapy.<sup>23</sup> Ii *et al.* repeated the food recall assessment after a 4-month period.<sup>24</sup> Tomedi *et al.*, Alves *et al.*, Shrestha *et al.* and Kheradmand and Kheradmand utilised food frequency questionnaires as a method of assessing intake with Tomedi *et al.* also utilising biomarkers to assess micronutrient and essential fatty acid levels.<sup>9, 26-28</sup>

The majority of included papers included an assessment of both macro and micronutrient and resulting

TABLE 1 Characteristics of studies investigating nutritional intake in opioid replacement therapy (ORT) patients

Study	Origin	Study design and methods	Population	Patient sample size	Nutritional aspect investigated <sup>a</sup>	Outcomes
Kolarzyk et al. 2005 <sup>23</sup>	Poland	Cohort study utilising 24-h food recall at baseline and after 4 years of ORT	ORT patients	30	Macro and micronutrient intake	Intake of micronutrients and carbohydrates below recommended levels
Ii et al. 2016 <sup>24</sup>	United Kingdom	Cross-sectional study utilising 24-h food recall	ORT patients	25	Macro and micronutrient intake	Intake of fibre, selenium and potassium were significantly lower than recommended levels
Waddington et al. 2015 <sup>25</sup>	Australia	Cross-sectional study utilising a single 24-h food recall	ORT patients	66	Macro and micronutrient intake and supplement intake	Irregularity in macronutrient contribution to energy and intake of micronutrients below recommended levels
Tomedi et al. 2012 <sup>26</sup>	United States	Cross-sectional study utilising food frequency questionnaire and micronutrient and essential fatty acid biomarkers assessment in pregnant ORT patients	Pregnant ORT patients	22	Macro and micronutrient intake and nutritional biomarkers	Significantly higher energy intake and poor nutritional status compared to control group
Kheradmand and Kheradmand 2020 <sup>27</sup>	Iran	Cross-sectional study utilising food frequency questionnaire	ORT patients	198	Food group servings	ORT patients had an increased consumption of simple carbohydrates and were deficient in healthy food intake
Alves et al. 2011 <sup>9</sup>	Portugal	Cross-sectional study utilising food frequency questionnaire	ORT patients	49	Food group servings, macronutrients, fibre, calcium and iron	ORT patients did not consume the minimum recommended servings of fruits, vegetables and grains and had an increased consumption of sweets
Shrestha et al. 2018 <sup>28</sup>	United States	Cross-sectional study utilising food frequency questionnaire	ORT patients	53	Macro and micronutrient intake	ORT patients had significantly higher mean energy intake. Patients also demonstrated intake of vitamin D, vitamin E, iron, and folate below the estimated average requirements

<sup>a</sup>Macronutrients include fat, proteins and carbohydrates. Micronutrients include all vitamin and mineral products.



energy intake as determined by food consumption.<sup>23-26,28</sup> Kheradmand and Kheradmand did not provide an analysis of nutrient levels.<sup>27</sup> Shrestha et al. and Waddington et al. also assessed reported nutritional supplement intake in their included patient groups.<sup>25,28</sup>

The STROBE checklist was utilised to assess the quality of the seven included papers. Each of the included studies utilised an observational, quantitative design. All the included articles met the STROBE checklist criteria for providing a clear balanced title and abstract, and also background and rationale within the introduction. In addition, each of the included papers included clear objectives and a statement of aims.

In relation to study methods, in all cases, study design was adequately presented however details of recruitment dates were not defined in two (28%) of the seven papers.<sup>9,27</sup> Participant eligibility was described in each of the papers and on all occasions the included population appeared to have been recruited appropriately. It was unclear in 2 (28%) of the included articles whether the chosen methods for measuring outcomes were appropriate due to single administration or minimal repetition of the utilised tools.<sup>25,27</sup> Additionally, five (71%) of the included articles were found to either not account appropriately for confounders or bias in study design or analysis of this was unclear.<sup>9, 24-27</sup> Five (71%) of the papers did not contain analysis of the potential bias in data collection.<sup>9, 24-27</sup> Statistical methods were adequately described in all but one of the included papers.<sup>23</sup>

On review of the results of each of the included papers, participant data and descriptive data were found to be adequately described across all studies. Six (85%) of the included papers met the criteria for having complete outcome data.<sup>9, 23, 25-28</sup> All papers included a summary of key results and provided a discussion of the generalisability of their respective results. Two (28%) of the papers lacked proper discussion of limitations and potential sources of bias.<sup>9,23</sup> Finally, the source and role of funds was not available for two of the included papers.<sup>23,27</sup>

In addition to the above analysis, it is noted that, ethical consideration was not clearly recorded in 2 (28%) of the included papers and other sources of potential bias include the low sample size observed in some of the studies and the inability for researchers to blind participants to the goals of their research.

All the included papers were considered to have produced valuable research.

A theme arising from review of the included studies was that nutritional intake varied between sexes but also that neither sex generally met the recommended values. Kolaryzk et al. found that women were observed to have a consumption of macronutrients that resulted in energy intake above recommended values.<sup>23</sup> Waddington et al. observed potential deficiencies in micronutrients and

irregularities in energy intake from macronutrients across the sexes.<sup>25</sup> The results from Ii et al. also showed that intake differed between male and female patients however both sexes were observed to have potentially deficient intake of selenium, potassium, and fibre.<sup>24</sup>

In addition, Waddington et al. found that women reported potential insufficient intake of several vitamins including vitamin A, vitamin E and thiamin. Conversely, male intake of vitamins appeared to be more in line with Australian Government dietary guidelines.<sup>25</sup> Both female and male patients were observed to be consuming a high level of sodium and females were observed to have a low intake of both calcium and iron.

An increased intake of saturated fats and of fatty acids was also observed in both of the studies by Waddington et al. and Ii et al. with the latter concluding that increased attention to nutritional outcomes in this patient group suggested.<sup>24,25</sup>

In terms of investigation food group intake, Kheradmand and Kheradmand observed that intake of foods considered to be healthier, such as complex carbohydrates, vegetables and fish was low, whereas consumption of sweets was comparatively high.<sup>27</sup> The authors concluded that further investigation into appropriate diet in long-term opioid replacement therapy patients was required. Similarly Alves et al. observed that the intake of opioid replacement therapy patients did not meet the recommended daily intakes of the number of servings of fruit, vegetables or grains as per the food pyramid.<sup>9</sup> Additionally, individuals' daily consumption of sweets was high, at an average of over five servings per day.<sup>9</sup>

In those included papers that utilised control group comparisons, Shrestha et al. found that mean energy intake was significantly higher in individuals undertaking opioid replacement therapy compared to controls.<sup>28</sup> Comparatively, Tomedi et al. observed that pregnant women undergoing opioid replacement therapy reported an energy intake that was significantly higher than the non-opioid replacement therapy women (control group), with the opioid replacement therapy patients consuming more energy from sweets.<sup>26</sup> Intake of micronutrients and polyunsaturated fatty acids did not differ between opioid replacement therapy patients and the control group.<sup>26</sup>

The authors across all included papers concluded that opioid replacement therapy patients appeared to have poor nutritional intake and that proactive provision of nutritional interventions may benefit this population.

## 4 | DISCUSSION

This systematic review was conducted to investigate the current evidence regarding the nutritional intake of

patients undergoing opioid replacement therapy. Seven papers were identified that examined intakes of opioid replacement therapy patients through various methods. In summary, the review found a small body of evidence suggesting the nutritional intakes of opioid replacement therapy patients are lacking in various micronutrients and that opioid replacement therapy patients have unbalanced intakes of macronutrients. Several biases were observed in the included papers and therefore the findings should be interpreted with caution.

Three different methods of assessing opioid replacement therapy patients' nutritional intake were observed in the included studies: measurement of biomarkers, food frequency questionnaires and 24-h food recall.

It is suggested that measurement of biomarkers of certain nutrients presents the most accurate indication of an opioid replacement therapy patient's nutritional status as both food frequency questionnaires and 24-h food recalls rely on memory and cognitive function for accuracy, which can be negatively impacted by opioid replacement therapy.<sup>25,27</sup> Further, both the recall and questionnaire may be subject to recall bias and underreporting which has been reported to occur at levels of up to 30% of 24-h food recalls performed.<sup>25</sup> In addition to the issues of reliance on memory, the utilisation of a food frequency questionnaire is limited in ability to provide a measurement of energy intake.<sup>26</sup>

The 24-h food recall method is an accurate tool for assessing nutritional intake with research supporting several repetitions of the recall are required to ensure accuracy.<sup>30,31</sup> Specifically, previous research has suggested that the use of three repetitions performed on varying days of the week is necessary to provide an accurate depiction of an individual's actual dietary intake.<sup>30</sup> Both Ii et al. and Kolarzyk et al. conducted multiple food recalls.<sup>23,24</sup> Kolarzyk et al. present results obtained from three recall sessions conducted over separate, non-consecutive days of the week.<sup>23</sup> Similarly, Ii et al. conducted five recalls over varying days of the week.<sup>24</sup> Ii et al. further increased the accuracy of the obtained data by repeating their methods after a 4-month period to account for any dietary changes.<sup>24</sup> Comparatively, Shrestha et al. and Waddington et al. only implemented a single 24-h recall to assess intake and therefore the results obtained may not provide an accurate representation of the intake of this population.<sup>25,28</sup> Collection of data over multiple days of the week to increase accuracy is likely to be more achievable in this population due to their tendency to receive opioid replacement therapy on a daily basis. It should be noted, however, that the availability of subcutaneously dosed buprenorphine therapy may alter the ability to collect such data.

There is a lack of control data across the majority of included papers. Only Tomedi et al. and Shrestha et al. utilised a control group to provide a comparison of nutritional intake, with the other included papers comparing the intake of opioid replacement therapy patients to national recommended values.<sup>26,28</sup> It is therefore possible that the results of the five included papers without control groups in this review are indicative of nutritional intake issues that are not specific to the opioid replacement therapy population and may be representative of broader populational issues.

Most of the included papers provided a cross-sectional view of opioid replacement therapy patient nutritional intake. It is therefore unclear if the reported nutritional issues are due to opioid replacement therapy or if they existed in this patient group prior to therapy and may be attributable to other demographic factors. Research has illustrated that similar nutritional issues may exist in the general population and are contributed to by such factors as income level, education and race and therefore may not be specific to this patient group.<sup>32</sup> Consequently, future research directly comparing the nutritional intake of a non-opioid replacement therapy population with opioid replacement therapy patients may be necessary. Kolarzyk et al. examined patient nutritional intakes prior to opioid replacement therapy and then followed participants up 4 years after commencing opioid replacement therapy treatment and observed an improvement in nutritional intake.<sup>23</sup>

Nutritive intake plays an important role in recovery and maintenance of optimal health. Poor nutritive intake has been shown to lead to barriers to ceasing opioid consumption and good nutritional education may assist opioid withdrawal.<sup>7</sup> The outcomes of the included papers in this systematic review present a depiction of a population that is at risk of several nutritional deficiencies which subsequently may be playing a negative role in these patients' recovery and withdrawal processes.

In terms of macronutrients, a higher fat intake was observed in the research undertaken by Kolarzyk et al. and Ii et al.<sup>23,24</sup> Both Kolarzyk et al. and Waddington et al. observed higher intakes of proteins than recommended values.<sup>23,25</sup> Tomedi et al., Alves et al. and Kheradmand and Kheradmand noted an increased consumption of sweets, likely consisting of high levels of fats and sugars (carbohydrates).<sup>9, 26, 27</sup> An increased consumption of sweet products is commonly recognised in opioid dependant individuals.<sup>10</sup> Further research into the underlying mechanism for this preference is warranted.

As a result of this irregular consumption, energy gained from macronutrient intake appeared abnormal in the outcomes of Alves et al., Waddington et al., Shrestha et al., Kolarzyk et al., and Tomedi et al. (obtained via

food frequency questionnaire).<sup>9,23,25,26,28</sup> Energy intake was observed to be low in the study by Waddington et al., however, was found to be high in the papers by Shrestha et al., Kolarzyk et al. and Tomedi et al.<sup>23,25,26,28</sup> Appropriate energy intake is important for ongoing functions of cell metabolism and muscle performance.<sup>33</sup> Low energy intake may impair ongoing bodily functions and high energy intake may contribute to overweight and other associated comorbidities.<sup>33</sup>

A wide range of potential micronutrient intake deficiencies were observed across the included research. However, it is not clear from the available research if specific nutrient deficiencies are occurring regularly across this population. Rather, the research has shown that there appears to be a selection of nutritional issues occurring in these individuals. In terms of specific micronutrients issues that were observed across multiple studies, of note, low iron was observed in female participants in the results of Shrestha et al., Kolarzyk et al., Waddington et al., Tomedi et al. and Li et al.<sup>23-26,28</sup> Waddington et al. and Kolarzyk et al. identified issues with calcium intake.<sup>23,25</sup> Sodium intake was high in the studies by Waddington et al. and Li et al.<sup>24,25</sup> Both Waddington et al. and Li et al. observed low intakes of selenium and potassium in opioid replacement therapy patients.<sup>24,25</sup> Further research is necessary to understand whether these micronutrient issues are able to be specifically associated with opioid replacement therapy populations.

The above-mentioned irregularities in micronutrient consumption are likely to have implications for opioid replacement therapy patient health. Vitamins play an important role in energy production and immune function whilst minerals are necessary for growth, bone health and fluid balance. Opioid replacement therapy patients have been shown to be at greater risk of poor nutritional status and malnourishment.<sup>34,35</sup> Poor nutritional status as a result of irregular intake of micronutrients can place individuals at risk of a range of comorbidities including cardiovascular disease, respiratory disease, diabetes and cancers.<sup>27</sup>

Each of the papers identified that this population may be suffering potential nutrient deficiencies due to unbalanced food consumption. However, it is not clear from the available research if there is any one single nutrient deficiency occurring in this population. There exists a consensus that further research in this area is necessary and that increased attention to nutritional intake; provision of supplementation; and increased nutritional education and advice may be beneficial in improving health outcomes in this population.

Several factors may be affecting the ability to determine a consistent pattern of nutrient insufficiencies in opioid replacement therapy patients. Food consumption,

food preferences and subsequent nutrient intake, is determined by many influences. Such determinants of food intake include internal factors (sensory features), personal-state factors (biological features, habits and experiences), cognitive factors (knowledge and skills), as well as sociocultural factors.<sup>36</sup> Gaining an understanding of how these factors differ between opioid replacement therapy patients internationally is integral to understanding the full picture of nutritional health in these individuals. Further, understanding whether the nutritional health of opioid replacement therapy patients differs to the general population is also necessary. Future research in this area is necessary to understand the factors affecting opioid replacement therapy patient nutritional health and whether their nutrient intake differs from that of the general population. Further, utilising consistent methodology to research the intake of these individuals is necessary to understand which (if any) nutrients these individuals are at risk of lacking.

In terms of limitations, a more extensive review of the literature may be conducted through inclusion of non-English language papers and removal of a specific timeframe for publication of included papers. Due to the low number of papers that met the eligibility requirements, the included papers are not necessarily of a high methodological quality. Several included papers fail to account for external factors that may affect opioid replacement therapy patient's nutritional intake and do not provide a comparative patient group.

This systematic review found that there is currently little research investigating the nutritional intake of individuals undergoing opioid replacement therapy. The existing research paints a picture of poor nutrition-related health outcomes in this population and is suggestive of the need for increased intervention in this area.

Poor nutritional intake has implications for chronic comorbidities and may negatively impact ongoing patient health and addiction recovery. This review highlights the need for increased attention to nutritional intake and interventions in this vulnerable patient group.

## AUTHOR CONTRIBUTIONS

FW and MN developed the initial research question and conceptualised the systematic review and methodology. FW, BW and VO contributed to literature searching, screening, data extraction and quality assessment. FW drafted the manuscript. MN and JT contributed to data interpretation and provided critical feedback on the manuscript.

## CONFLICT OF INTEREST


The authors have no conflicts of interest to declare.



## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analysed in this study.

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